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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,842	MASLIAH ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-8 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5,7,8 and 12-15* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1. The amendment filed 2-2-04 has been entered into the record and has been fully considered. Claims 1-3, and 9-11 are canceled. Claims 4-8 and 12-15 are pending.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Election/Restriction

4. Applicant's election of Group II, claims 4-8 in the Paper of 9-2-03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Newly submitted claims 11-15 are directed to the invention of Group II and are under examination.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 4-5, 7-8 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter

rejection. Applicants new claims recite "A method for screening for treatments for neurodegenerative disease comprising inducing aggregation of amyloidogenic proteins; exposing amyloidogenic proteins to a treatment; measuring aggregation of NACP/α-synuclein and measuring aggregation of NACP/α-synuclein to test for a decrease in aggregation, wherein the decrease is indicative of an effective treatment." Applicant's have not provided support for the claim amendments. Further, new claims 11-13, recite "wherein the aggregation is induced by oxidative stress," "wherein the treatment comprises an agent to promote the expression of anti-amyloidogenic proteins," and "wherein the anti-amyloidogenic protein is β-synuclein." However, applicant's have not provided supoort for the new claim recitations as recited and the Examiner fails to find apparent support. Thus, the newly recited methods constitute new matter absent evidence of support in the specification as originally filed. The new matter is noted to extend to Applicant's 371 priority document of PCT /US99/23134, 10-6-1999 and the provisional 60/103,310, 10-6-1998 as filed. As set forth below, priority therefore cannot be established. As the instant specification is a mirror of the 371 filing, Applicant's response should address how support for the claimed methods may be found within instant application as well as the provisional application of 60/103,310 if Applicant's are to obtain the benefit of the earliest priority date. Applicants should particularly address all amendments to the claims as submitted 9-2-03 including all new limitations.

Applicants argue as set forth in pp. 6-10 of the 2-2-04 response.

Applicant's arguments at pp. 6-10 of the 2-2-04 response have been fully considered but are not persuasive. In particular, Applicants point to support for claim 4

within the provisional application at pp. 17-28 and Example 1, p. 22, 4F, of the specification. While such supports that ferric ion and ferrous ion with hydrogen peroxide is capable of inducing aggregation, it is noted that such does not apparently address the scope of the claim as directed to "an oxidizing agent" or to claim 5 as directed to "a mixture of metal-ions and hydrogen peroxide". While iron catalyzed oxidation is noted to be effective in the provisional, the provisional and specification further note that other metals were ineffective in promoting aggregation, see in particular p. 7 of the Hashimoto et al., reference in which cupric and manganese ions and hydrogen peroxide alone were incapable of promoting NACP/alpha-synuclein aggregation. Further as to the recitation of claim 5, there is no apparent evidence other than with ferrous ion and hydrogen peroxide that the combination of a mixture of metal-ions and hydrogen peroxide would be effective to promote aggregation of NACP/alpha-synuclein. Thus, while iron catalyzed oxidizing agents are apparently supported as in claim 6, the broad recitation of an oxidizing agent, and combination of hydrogen peroxide with a mixture of metal-ions (other than with ferrous ion) appears to be new matter absent further support for these broader recitations.

7. Claims 4-5, 7-8 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing aggregation of alpha-synuclein via exposure to a product of an iron-catalyzed oxidative reaction as in claim 6, does not reasonably provide enablement for inducing such aggregation via exposure to any oxidizing agent or mixture of metal-ions and hydrogen peroxide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Applicant's specification teaches the exposure to ferric ion alone and ferrous ion with hydrogen peroxide were sufficient to provide for alpha-synuclein aggregate formation. However, the specification further teaches that cupric and manganese ions and hydrogen peroxide alone were incapable of promoting NACP/alpha-synuclein aggregation. The art and specification are silent as to what other oxidizing agents are capable of inducing alpha-synuclein with the exception of beta-amyloid as noted below which has been shown to exhibit oxidative damage in neurons and to stimulate aggregate formation of alpha-synuclein. Thus, there is no apparent evidence other than with ferrous ion and hydrogen peroxide that the combination of a mixture of metal-ions and hydrogen peroxide would be effective to promote aggregation of NACP/alpha-synuclein. Thus, while iron catalyzed oxidizing agents are apparently supported and in scope with claim 6, the broad recitation of an oxidizing agent, and combination of hydrogen peroxide with a mixture of metal-ions (other than with ferrous ion) as in claim 5 appears to be beyond the scope of enablement provided by the specification and prior art.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the invention in full scope with the claims without further undue experimentation.

Priority

8. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Instant application claims priority from 60/103,310 filed 10-6-1998. Applicants should note the new matter rejection of record. With respect to the priority document of 10-6-1999. Support for the claim recitations is similarly not found within the prior '310 provisional application. Accordingly the effective filing date awarded instant claims is the date of 11-13-01 absent evidence for support in both instant application (371 of PCT/US99/23134, 10-6-1999 and the provisional 60/103,310, 10-6-1998 as filed.

Applicants traverse the priority determination as set forth above in the new matter rejection. As noted above by the Examiner, claim 6 appears to be supported by the provisional application. However, as set forth above, evidence of support is not established for the contemplation of "oxidizing agents" and for "a mixture of metal-ions and hydrogen peroxide" as newly recited. Thus, the priority date of claims 4-5, 7-8 and 12-15 is the date of 11-13-01 absent further support in the specification and priority document as filed.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claim 4 is rejected under 35 U.S.C. 102 (a) and (e) as being anticipated by Biere et al., US Patent 6,184,351 filed 9-24-1999 and issued 2-6-2001 or in the alternative, under 35 U.S.C. 103 as obvious over Biere et al., US Patent 6,184,351 filed 9-24-1999 and issued 2-6-2001.

Biere et al., teach alpha-synuclein super mutants that accelerate alpha-synuclein aggregation thus, Biere teaches a method "comprising inducing aggregation of amyloidogenic (alpha-synuclein) proteins" as claimed. Biere et al., teach that Parkinson's disease (PD) is a neurodegenerative disorder which is pathologically characterized by the presence of intracytoplasmic Lewy bodies, the major component of which are filaments consisting of alpha-synuclein, see in particular abstract. Biere et al., teach an invention that provides alpha.-synuclein mutants which accelerate alpha-synuclein aggregation and can thus be utilized for transgenic animal production and generation of the first progressive PD model. Biere et al., also provide an in vitro aggregation assay which can be utilized to identify alpha.-synuclein nucleation inhibitors for the treatment of PD. Thus, Biere teaches "A method for testing for treatments for neurodegenerative disease" as claimed. The method of Biere et al., includes exposure to a potential nucleation-affecting agent, see in particular claim 4 and thus Biere et al., teaches a method wherein the amyloidogenic proteins are induced to aggregate and then "expose(ed) to a treatment", wherein the comparison of the amount of aggregated α-synuclein is measured and assessed. As set forth in Biere et al., the assay is for alpha-nucleation inhibitors and such inhibitors are noted to be useful in the treatment of pathological conditions such as Parkinson's. The inhibitors are from a panel of drug candidates and occurs wherein the samples are compared to assess treatment efficacy as indicated by levels of aggregation in samples with test treatment. Thus, Biere et al., teach the steps of "inducing protein aggregation in a first sample comprising

NACP/alpha-synuclein, exposing the first sample to a treatment, inducing protein aggregation in a second sample comprising NACP/alpha-synuclein, measuring an aggregation level of NACP/alpha-synuclein in the first sample and the second sample and comparing the aggregation level of NACP/alpha-synuclein in the first sample with the aggregation level of NACP/α-synuclein in the second sample wherein less aggregation in the first sample is indicative of an effective treatment." Thus the Biere reference teaches all of the limitations of claim 4 but does not teach that the alpha-synuclein super mutants are suitable oxidizing agents, i.e., where the super mutants exhibit or provide for oxidizing effects in the cell. The Examiner is unable to determine whether or not exposure of the alph-synuclein super-mutants to the cell provides for the specific property of exposing the samples to an oxidizing agent. With these conditions, where exposure to the alpha-synuclein supermutants promotes aggregation of NACP/alpha-synuclein and thus seem to be identical in characteristics or properties to that claimed as exposing to an oxidizing agent to promote aggregation, the USPTO has insufficient resources and facts to determine whether the respective exposure is "inherently the same" or "obvious" because the Examiner cannot determine whether the exposure of the alpha-synuclein super-mutants acts as an oxidative agent. The Examiner is not in a position to determine inherency or obviousness because the record does not establish how the steps are the same or differ. Since the record does not allow such determination, the burden shifts to Applicants to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of In re Best 195 USPQ 430, 433 (CCPA 1977).

11. Claims 4, 7-8 and 12-15 are rejected under 35 U.S.C. 102 (b) as being anticipated by Jensen et al., Biochem. J., 323:539-546, Apr. 15, 1997 as evidenced by Harris et al., Experimental Neurology, 1995, 131(2):193-202.

Jensen et al., teach that, "the identification of peptides that bind Abeta might open new possibilities for preventing the formation of AD plaques," the major pathology associated with Alzheimer's disease, see in particular pp. 545, column 2, lines 5-14. Jensen's "strategy is to identify small peptides that inhibit Abeta self-aggregation and the formation of complexes between Abeta and synucleins and their fragments....Future studies should show whether peptides derived from synucleins might prevent aggregations and whether they might be used as lead substances for the construction of drugs." Thus, Jensen et al., teach a screening based method for treatments of Alzheimer's type neurodegenerative disease based upon the identification of molecules that inhibit aggregation of Abeta and synucleins. Jensen et al., teach methods for inducing aggregation of amyloidogenic proteins, see in particular Experimental, pp. 540, column 2, lines 24-44, and Results, Aβ binding to α- and β- synuclein, pp. 541-542, Figures 1-3. The amyloidogenic proteins were subject to treatment with BS3 crosslinker and the specificity of binding to alpha –synuclein was measured via SDS-PAGE analysis. Other treatments include incubation or exposure to Abeta, NAC, SDS, or β-synuclein. Jensen is silent as to Abeta being an oxidative agent. However, Harris et al., teach direct evidence of oxidative injury produced by beta-amyloid peptide. Thus, as evidenced by Harris, the contact of Abeta as taught by Jensen is equivalent to exposure to an oxidizing agent which as noted by Jensen provides for aggregation of NACP/alpha-synuclein. Jensen also teaches such measurements in the presence or absence of β-synuclein, Aβ and NAC. It was also shown that α-synuclein can form homodimers or heterodimers with β-synuclein, effectively teaching that β-synuclein can compete with α-synuclein for binding, see in particular Figure 4, and pp. 542, columns 1-2 paragraph spanning. Thus, Jensen teaches, "exposing amyoidogenic proteins to a treatment, measuring aggregation of α-synuclein to test for a decrease in aggregation

wherein a decrease is indicative of an effective treatment." Further, Jensen notes that the complex formation is SDS sensitive. Thus, Jensen teaches that SDS, Aβ peptide, NAC and β-synuclein each compete or serve to inhibit α-synuclein aggregation and binding. Each of these results exhibit competition for α-synuclein aggregation/binding and thus are tests for decreases in aggregation as the molecules inhibit the formation of complexes. Moreover, the peptides are noted to aggregate and thus may be considered treatments as they are exposed to the amyloidoginic proteins as claimed. As claimed in claims 12-13 the method of Jensen includes treatment including exposure to the agent beta-synuclein and thus the reference encompasses the beta-synuclein agent that promotes the expression of anti-amyloidogenic proteins. Thus, Jensen et al., teach "A method for testing treatments of neurodegenerative disease comprising" the steps of "inducing protein aggregation in a first sample comprising NACP/alpha-synuclein by exposing a first sample to an oxidizing agent, exposing the first sample to a treatment, inducing protein aggregation in a second sample comprising NACP/alpha-synuclein by exposing a second sample to the oxidizing agent, measuring an aggregation level of NACP/alpha-synuclein in the first sample and the second sample and comparing the aggregation level of NACP/alpha-synuclein in the first sample with the aggregation level of NACP/α-synuclein in the second sample wherein less aggregation in the first sample is indicative of an effective treatment." Thus the reference teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 4-5, 7-8 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al., NeuroReport 10:717-721, 1999 alone or alternatively in view of either Biere et al., US Patent 6,184,351 filed 9-24-1999 and issued 2-6-2001 or Jensen et al., Biochem. J., 323:539-546, Apr. 15, 1997.

Hashimoto et al., teach oxidative stress stimulated by iron and peroxide in the formation of amyloid-like aggregates of α-synuclein. Hashimoto et al., also teach that such synuclein plaques are a major pathology in the brains of patients with Parkinson's and Lewy Body disease. Hashimoto et al., further teach that the iron chelator deferoxamine was able to inhibit the iron-catalyzed oxidative reaction that stimulated aggregation, see in particular abstract, Results, pp 718-20 and Figures 1-2. Thus, Hashimoto et al., teach a method including "inducing aggregation of amyloidogenic proteins, exposing amyloidogenic proteins to a treatment and measuring aggregation of NACP/alpha-synuclein and testing for a decrease in aggregation. The treatment of

deferoxamine is noted to be a treatment that decreases aggregation.

Hashimoto et al., fall short of suggesting that such assays could be used for the purpose of screening for treatments for neurodegenerative disease and that such decreases in aggregation would be indicative of effective treatments for neurodegenerative disease. Such are the claim recitations within the preamble and outcome of the claimed method.

However, one of skill in the art would have been motivated to use the assay of Hashimoto et al., in a screen for molecules capable of inhibiting alpha-synuclein aggregation for potential use as therapeutics to treat Parkinson's and Lewy body disease as the skilled artisan recognizes that the assay was effective and beneficial in finding a compound that was capable of inhibiting alpha-synuclein aggregation in vitro. The artisan is well apprised of the need for treatments which both inhibit oxidative stress in the brains of Parkinsons and Lewy body patients and the need for drugs to inhibit alpha-synuclein plaque formation because as Hashimoto evidences, alpha-synuclein plaques are recognized as the major pathology in such patient's brains. In particular, Hashimoto et al., teach within the discussion that "since iron promotes NACP/α-synuclein self-aggregation, it is possible that aberrant accumulation of ferric ion might act as a risk factor for the aggregation ...in the PD brain. Indeed, it has been suspected that the shift from ferrous to ferric ion may be a risk factor in PD. Riederer et al., showed that the ratio of ferric to ferrous ion in the substantia nigra of patients with advanced PD was remarkably increased compared with controls." In conclusion Hashimoto summarizes other data saying, "it is reasonable to speculate that

aggregation of NACP/α-synuclein is not only a result of increased ferric ions via oxidative reaction but can also be a trigger/stimulator of the iron-catalyzed oxidative reaction....The present study suggests that reactions involving oxidative stress might lead to aggregation of NACP/α-synuclein...It is then possible that this abnormally aggregated molecule might mediate the neurodegenerative process through mechanisms that remain unclear." Thus, the artisan is apprised of the links of oxidative stress in the formation of pathological alpha-synuclein aggregates in PD and Lewy body brains and would expect that inhibition of this mechanism would be effective in ameliorating alpha-synuclein plaque formation. Accordingly one of skill would be motivated to assess the a molecule resulting in the inhibition of alph-synuclein aggregation as one of therapeutic benefit in Parkinson's and/or Lewy body disease. One of skill in the art would have further expected success in identifiying potential treatments using such screening assays given the positive results of Hashiimoto in identifying molecules that inhibit alpha-synuclein aggregate formation given that Hashimoto teaches that such is the pathological basis of the plaque formations in patients with Parkinson's and Lewy body disease.

Should Hashimoto et al., with the discussion and relative skill in the art alone not be enough to convince applicants of the obviousness of the preamble recitation and indication of effective treatments with decreases in alpha-synuclein aggregation, further motivation is provided to the artisan for such screening assays via Biere and Jensen. These references as set forth above teach the use of the disclosed assay to screen for treatments for neurodegenerative disease and that agents that act as inhibitors or result

in decreases of aggregation are the compounds deemed to be appropriate for such treatments. Biere and Jensen each teach the same assay methods wherein the goal is to identify potential candidate treatments and/or therapeutics via assay for decreases or inhibition of α-synuclein amyloidogenic aggregation. Thus, Biere and Jensen provide the motivation to use the method of Hashimoto as a screening assay in which suitable inhibitors may be found as exemplified in the Hashimoto reference. Hashimoto teaches that an iron-catalyzed oxidative reaction induced via a mixture of ferric ion and peroxide is effective to increase aggregation of α-synuclein. Hashimoto et al., also teach defrroxamine inhibition of alpha-synuclein aggregate formation. Thus, in light of the methods of Biere and Jensen the artisan would have been motivated to use the alternative procedures of inducing aggregation using ferric ion and peroxide as demonstrated by Hashimoto or treatment with deferroxamine to inhibit alpha-synuclein aggregation. One of skill in the art would have expected success using such modification based upon the teachings of Hashimoto et al., that such treatment is effective to induce and/or inhibit α-synuclein aggregation. The cumulative references teach the required motivation and expectation of success for the screening method as claimed and thus the invention is obvious to the artisan in light of the reference teachings. The species of the genus of oxidizing agents and metal ions with peroxide are intrinsically provided.

Applicants argue that as only the Jensen reference is relevant prior art, the obviousness rejection falls.

Applicants arguments have been fully considered but are not persuasive

because as noted above priority is not granted to the noted claims and the references are available prior art.

Status of Claims

14. No claims are allowed.

15. The Examiner notes that the multiple rejections are not in conflict. Applicants bear the burden of showing that the full breadth of the claims were both supported and enabled by the provisional application in order to obtain full benefit of the priority date. Until such perfection, the noted prior art is properly applied.

Allowable Subject Matter

16. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach or fairly suggest alpha-synuclein aggregation via exposure to an iron-catalyzed oxidative reaction.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (571) 272-0887.

Sharon L. Turner, Ph.D.
April 28, 2004

Gary L Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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